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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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| HAYES,R | |
| **ART UNIT** | **PAPER NUMBER** |
| 1645 | |

DATE MAILED: 09/30/98

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**



☆U.S.GOVERNMENT PRINTING OFFICE 1995-319-826

| Office Action Summary | Application No. 08/826577 | Applicant(s) Dixit |
|---|---|---|
| | Examiner Vanyer | Group Art Unit 1645 |

*—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—*

**Period for Response**

A SHORTENED STATUTORY PERIOD FOR RESPONSE IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a response be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for response specified above is less than thirty (30) days, a response within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for response is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to respond within the set or extended period for response will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

**Status**

☐ Responsive to communication(s) filed on 2/6/97 and 4/2/97 and 8/15/97.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

**Disposition of Claims**

☒ Claim(s) 1, 22-23, 36-55 is/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☒ Claim(s) 42, 45, 48 is/are allowed.

☒ Claim(s) 1, 22-23, 36-41, 43-44, 46-47, 49-55 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claim(s) 1, 22-23, 36-55 were are subject to restriction or election requirement.

**Application Papers**

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119 (a)-(d)**

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

**Attachment(s)**

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 16½

☐ Interview Summary, PTO-413

☒ Notice of References Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

**Office Action Summary**

## DETAILED ACTION

1. This is a File Wrapper Continuation (FWC) of applicants earlier application, S.N. 08/404832, filed under 37 CRF 1.62; and is not a Divisional application. Therefore, prosecution continues from the parent application, wherein this Office action is directed to the merits of the invention elected in the parent application 08/404832, i.e., Group I, claims 1-5 & 22-23 (the protein species), in Paper No 7. Applicant's election of Group I in Paper No. 8 was acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election had been treated as an election without traverse (MPEP § 818.03(a)). It is noted that all nonelected claims were cancelled, except for claims 22-23 (the antibody species). Applicant is again reminded that this application, therefore, still contains claims drawn to an invention nonelected without traverse in Paper No. 8. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01. Further, copies of any prior art that was cited and/or relied upon in the parent application will not be resubmitted to applicant(s).

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reasons. For example, claims 43 & 44 now recite non-

contiguous fragments of SEQ ID NO: 2. It should be noted that 37 CFR 1.822(o) states that a sequence made up of one or more noncontiguous segments of a larger sequence or segments from different sequences shall be presented as a separate sequence. A new CRF and paper copy of the "Sequence listing" would then be required along with a new statement that these copies are the same and include no new matter. However, it appears that any such new sequence, as currently recited in claims 43 & 44, would constitute new matter, as discussed below.

3. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1645.

4. Claims 42, 45 & 48 are allowed.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Applicants' arguments filed 02/06/97 have been considered but are not found persuasive, as previously addressed in the advisory action of 3/5/97 (paper # 14).

7. Claims 1 & 36-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification provides a written description of a single species of CD40 binding protein (CD40bp), which is human CD40bp of SEQ ID NO:2. No other species of CD40bp are described, or structurally contemplated, within the instant specification. One skilled in the art also cannot reasonably visualize or predict what critical amino acid residues would structurally characterize the genus of mammalian CD40 binding proteins claimed (i.e., by amino acid sequence), based on the deficient description of the specification for what structurally constitutes any different CD40bp protein, or CD40bp from a non-mammalian species. Further, in that an infinite number of proteins can be envisioned to have an "apparent molecular weight of about 64 kD on SDS PAGE", this limited characteristic does not provide a sufficient description for the skilled artisan to structurally visualize what constitutes a "mammalian" CD40bp protein, versus what structurally constitutes any different protein of about 64 kD. Clearly, Applicant is not in possession of the genus of "mammalian" CD40 binding proteins because no contemplation of structure that defines such is described in the instant specification; thereby, not fulfilling the written description requirement under 35 U.S.C. 112, first paragraph.

8. Claims 1, 22-23, 36-41 & 43-44 are again rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time of the application was filed, had possession of the claimed invention, for the reasons made of record, and as follows.

No proper antecedent basis or conception for the negative claim limitation, "and does not specifically bind to a homologous tumor necrosis factor cell-surface receptor" (i.e., as it relates to claim 1), appears to be contemplated in context of that described within the specification at the time of filing the instant application, for the reasons extensively discussed during the interview of 1/23/97. For example, no such basis appears on pages 30-34 of the specification, as stated on page 5 of the response; thereby, constituting new matter.

No proper antecedent basis or conception in context of that disclosed within the specification at the time of filing the instant application is apparent for the recitations, "*further* comprises amino acids 266 to 366" or "comprises amino acids 49-79 as shown in SEQ ID NO:2" (i.e., as it relates to the specific amino acid ranges now claimed, and for joining these non-contiguous fragments of SEQ ID NO:2 into claims 43-44); thereby, constituting new matter.

No proper antecedent basis or conception in context of that disclosed within the specification at the time of filing the instant application is apparent for the recitation, "*at least one* RING finger domain", in that only a single "RING finger domain" is contemplated in the instant

specification for CD40bp proteins, as illustrated in Fig. 4C; thereby, constituting new matter for claim 36.

9. Claims 1, 22-23, 36-41, 43-44 & 54-55 are again rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to the human CD40 binding protein (CD40bp) of SEQ ID NO 2, and the specific fragment of SEQ ID NO:2 that comprises amino acid residue #s 297-567, for the reasons made of record, and as follows.

As previously made of record, the protein of claim 1 sets forth little structural and functional characteristics. Additionally, page 6 of the specification defines a CD40bp protein as including "[biologically] functional equivalents", and "equivalents which *vary the primary sequence of the protein*"; thereby, encompassing any putative mutation, addition, deletion, truncation, substitution, etc. to a human CD40bp protein. In contrast, the instant specification provides no guidance as to what critical amino acids are required for any generic and active CD40bp protein, or fragments thereof; nor what structurally defines any "dominant inhibitory fragment", as previously made of record (i.e., as it relates especially to claim 23). Moreover, random mutations, substitutions, additions, deletions and truncations to a structurally undefined protein would be predicted to adversely alter the biologically-active 3-dimensional conformation of the protein; thereby, resulting in an inactive CD40bp protein. For example, Rudinger teaches that "it is impossible to attach a unique significance to any residue in a sequence. A given amino acid will not by any means have the same significance in different peptide sequences, or even in

different positions of the same sequence"(see page 3). Rudinger further states on page 6 that "the significance of particular amino acid sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from case to case by painstaking experimental study". Therefore, the lack of guidance provided in the specification, as to what alterations can be tolerated to maintain a functional CD40bp polypeptide would prevent the skilled artisan from determining whether any random mutation or fragment or functional equivalent protein could be made that retains the desired function of the instant invention, without undue experimentation to determine otherwise. Thus, the specification does not sufficiently structurally characterize and enable the breadth of the polypeptide molecules currently encompassed by the claims, nor provides sufficient structural characterization to distinguish the polypeptides of the instant invention from any different polypeptide that possesses none of the desired functional properties of the invention; and as such, merely constitutes an invitation to experiment to discover how to make and use Applicants' invention.

By analogy, it was held in *Ex parte Maizel* (27 USPQ2d 1662 at 1665) that:

> Appellants have not chosen to claim the DNA [product] by what it is but, rather, by what it does, i.e., encoding either a protein exhibiting certain characteristics, *or* a biologically functional equivalent thereof. Appellants' claims might be analogized to a single means claim of the type disparaged by the Court of Customs and Patent Appeals in *In re Hyatt,* 708F.2d 712, 218 USPQ 195 (Fed. Cir. 1983). The problem with the phrase "biologically functional equivalent thereof" is that it covers any conceivable means, i.e., cell or DNA, which achieves the stated biological result while the specification discloses, at most, only a specific DNA [product] segment known to the inventor. Clearly the disclosure is not commensurate in scope with the claims [emphasis added].

Thus, because the claims encompass any "biologically functional equivalent" CD40bp product (i.e., especially, as it relates to new claims 54-55), the structurally deficient "mammalian" CD40bp proteins of the instant invention are also not enabled.

Lastly, claims 1, 22-23, 36-41& 54 recite negative claim language (i.e., "and does *not* specifically bind to a homologous tumor necrosis factor cell-surface receptor") which does not define the invention, but rather attempts to claim an invention by excluding what is not invented. However, the courts have held that negative limitations that exclude compounds do not meet the requirements of 35 U.S.C. 112 because it attempts to claim the invention by excluding what was not invented rather than what was invented. *In re Schechter, 205 F2d 185, 98 USPQ 144 (CCPA 1953).*

10. Claims 1, 22-23, 36-41 & 54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The negative claim language (i.e., "and does *not* specifically bind to a homologous tumor necrosis factor cell-surface receptor") does not define the invention, but rather attempts to claim an invention by excluding what is not invented; thereby, being indefinite. It should be noted that the courts have held that negative limitations that exclude compounds do not meet the requirements of 35 U.S.C. 112 because it attempts to claim the invention by excluding what was

not invented rather than what was invented. *In re Schechter, 205 F2d 185, 98 USPQ 144 (CCPA 1953).*

11. Claims 43-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the recitations, "comprising amino acids 266 to 366/ 49 to 79", because they do not further limit base claim 42, which "comprises amino acids 297 to 567".

12. Claims 39, 41, 49, 51 & 53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite and incomplete because it is unknown what is envisioned as the intended use of the pharmaceutical compositions, since none is recited.

13. Claims 22-23, 37 & 40-41 are rejected under 35 U.S.C. 102(a) as being anticipated by Rothe et al.

Rothe et al. teach a protein fragment comprising amino acids 384-424 of human TNF-R2 (pg. 683, 1st col.; Fig. 3), in which 30 out of 41 amino acid residues are identical to amino acids 447-487 of human CD40bp (see Fig. 4E). In that the specification defines CD40bp to include variations within the primary amino acid sequence (e.g. see pg. 6 of the specification), and because this peptide fragment is inherently immunogenic and within the C-terminal domain of CD40bp (i.e., a dominant inhibitory fragment of CD40bp; as it relates to claims 22-23), Rothe's TNFR2 fragment structurally meets all limitations of claims 22-23 & 37. In that this

immunogenic peptide is isolated in a composition comprising SDS and water (pg. 691, 1st col.), and because water is a pharmaceutically acceptable carrier, the limitations of claims 40-41 are also met.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Thursday, and alternate Fridays, from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached on (703) 308-4310. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
September 15, 1998

PAULA K. HUTZELL
SUPERVISORY PATENT EXAMINER